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(54) LIQUID FEEDING SYSTEM

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B01D 15/08 (2006.01)

(52) **U.S. Cl.** **210/198.2**

(57) **ABSTRACT**

This liquid feeding system has the first and second pumps each of which is provided with a plunger. Liquid sucked through each of the pump suction ports is discharged out of the discharging port through the first pump and/or second pump. Under the starting operation mode, the second pump is stopped and only the first pump is operated. When the discharging pressure at the discharging port reaches up to a predetermined value, the starting operation mode is changed over to the normal operation mode. Under the normal operation mode, the first pump is stopped and only the second pump is operated.

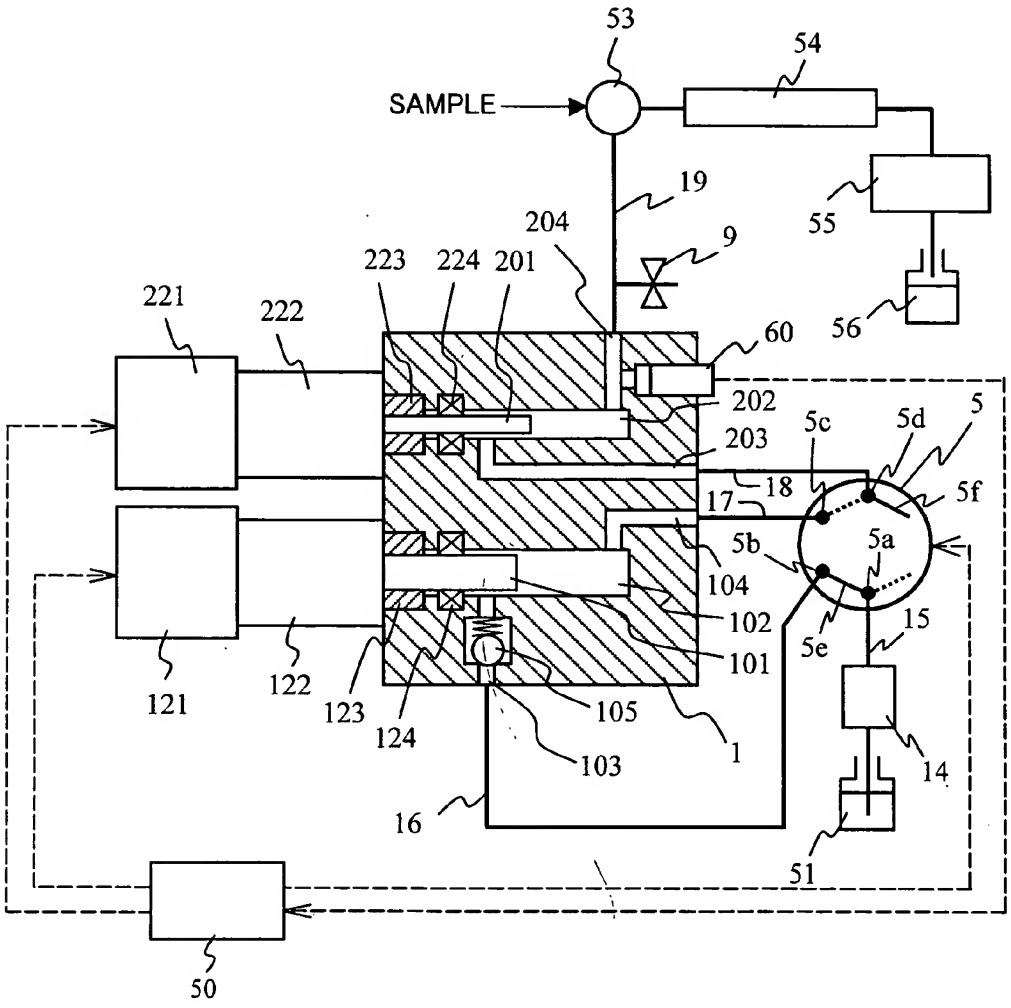

FIG. 1

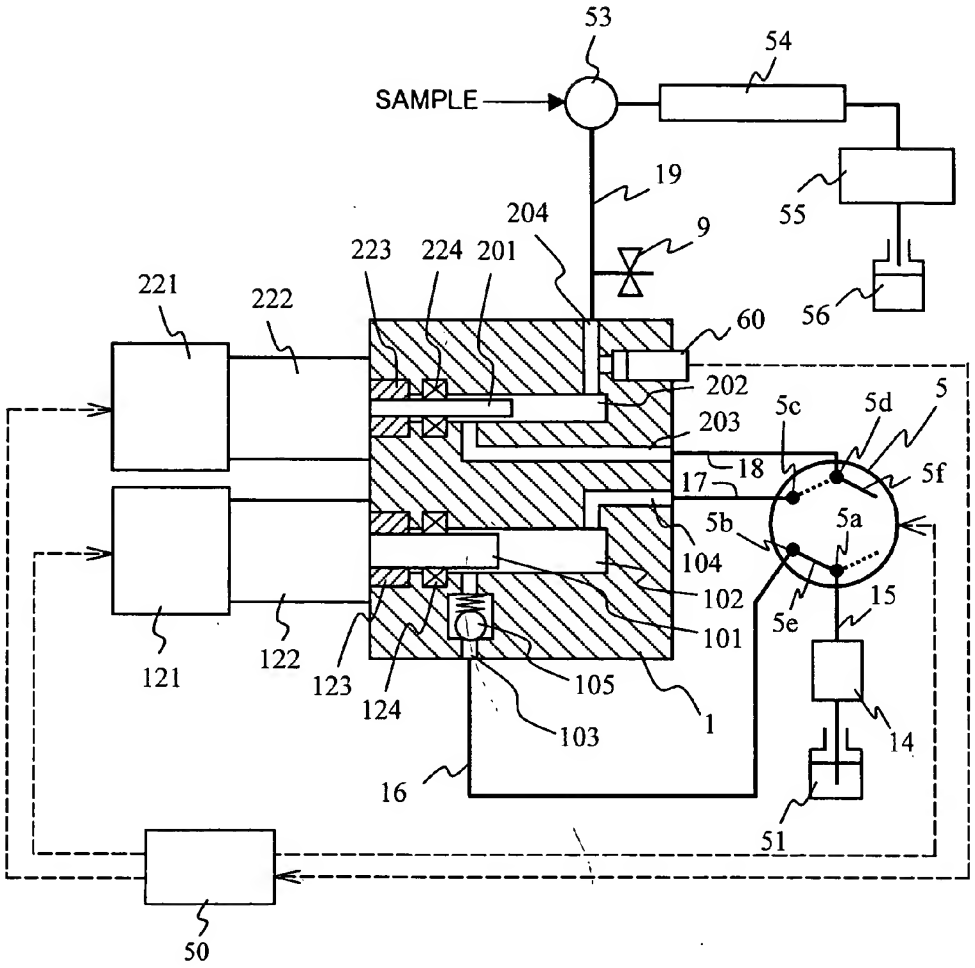
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FIG. 2

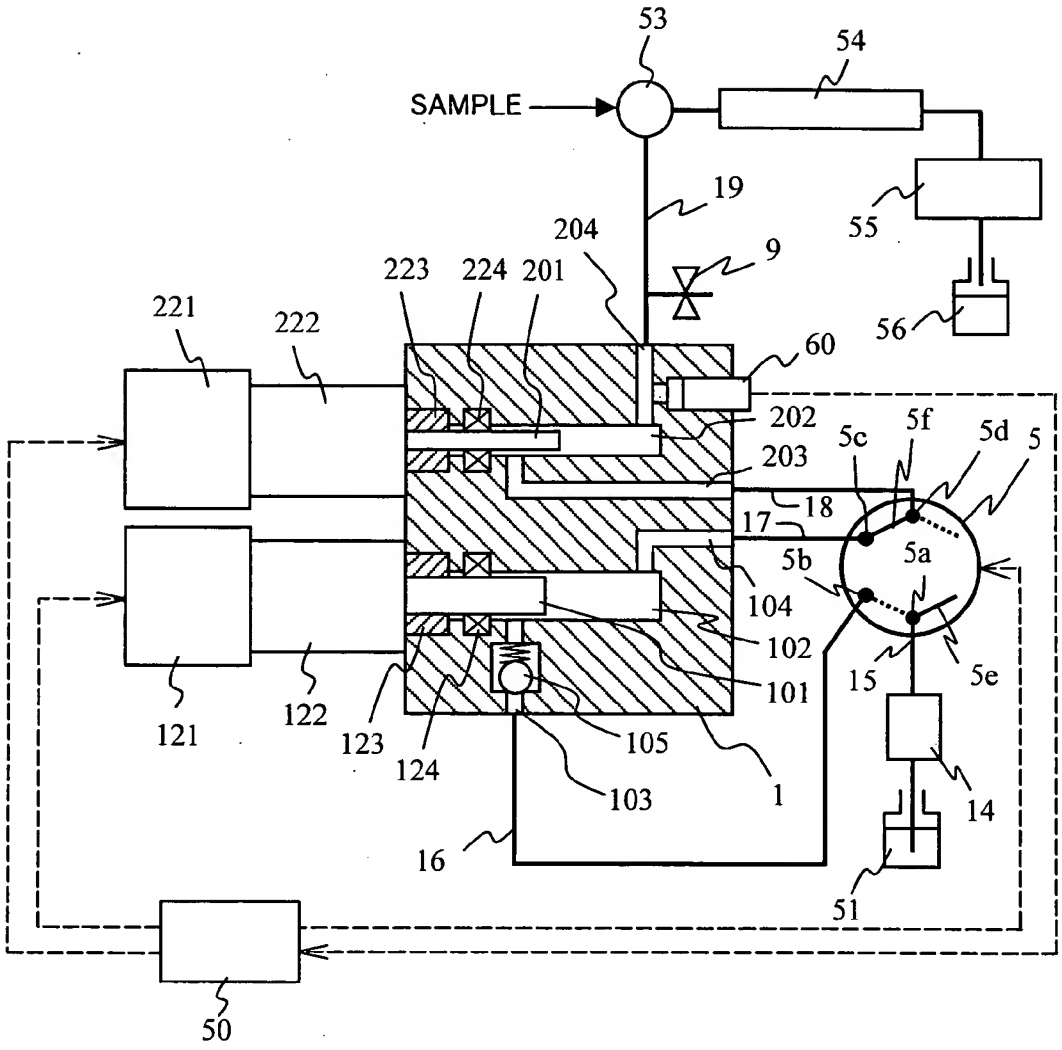
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FIG. 3 A

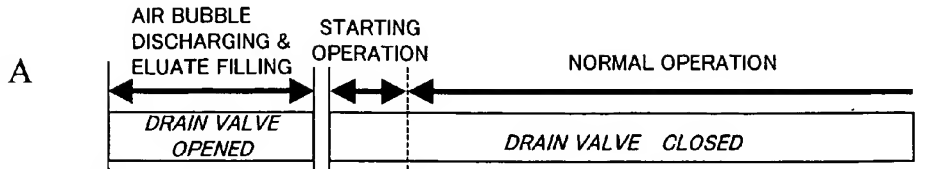


FIG. 3 B

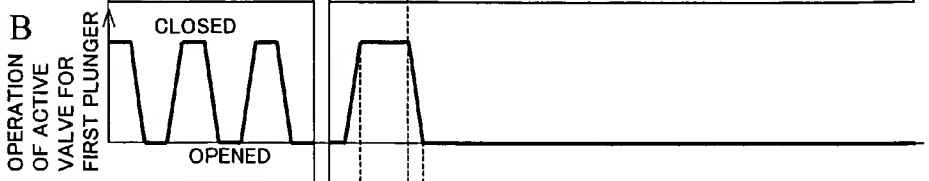


FIG. 3 C

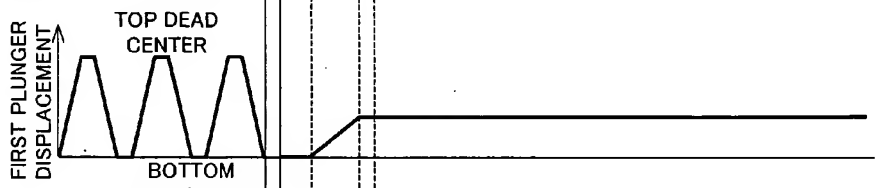


FIG. 3 D

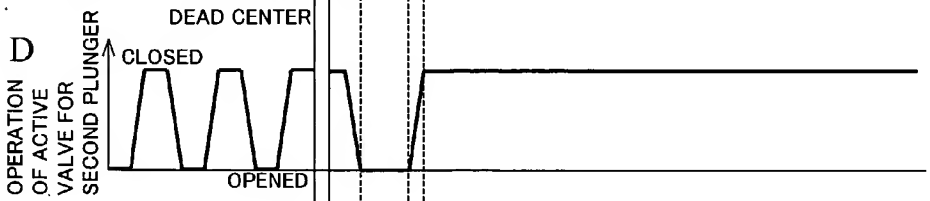


FIG. 3 E

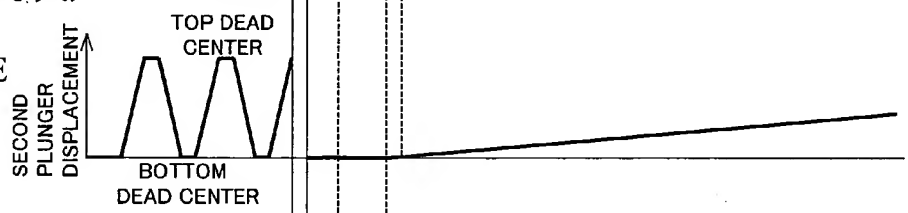


FIG. 3 F

FIG. 3 G

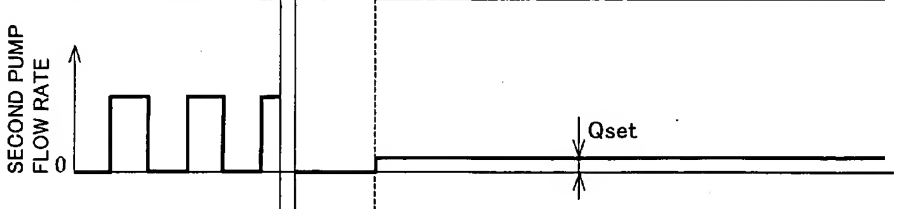
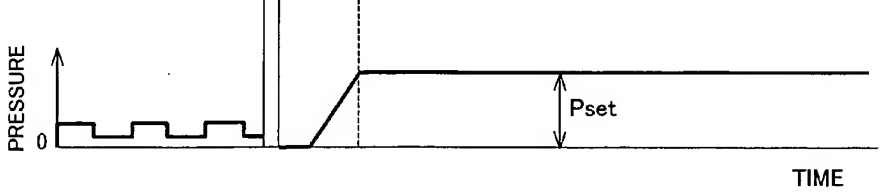


FIG. 3 H



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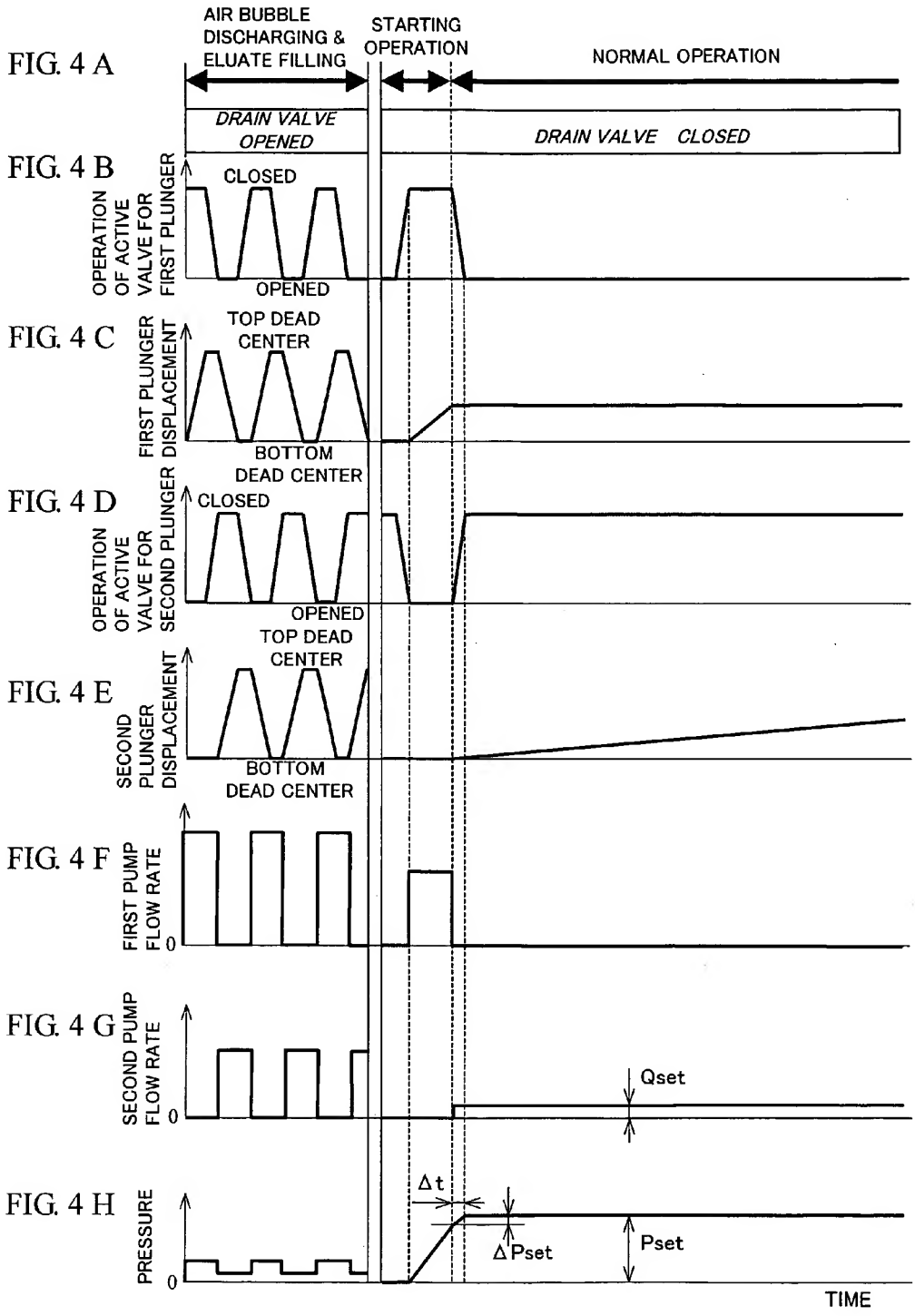

FIG. 4 B

FIG. 4 C

FIG. 4 D

FIG. 4 E

FIG. 4 F

FIG. 4 G

FIG. 4 H

FIG. 5

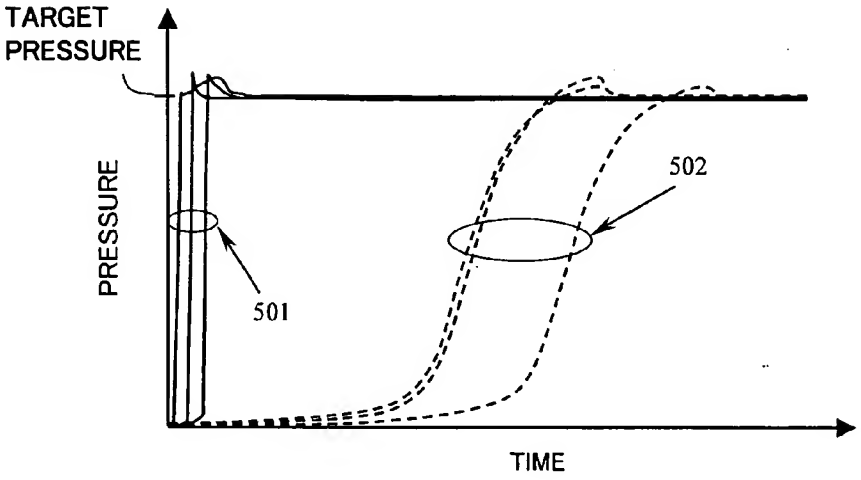
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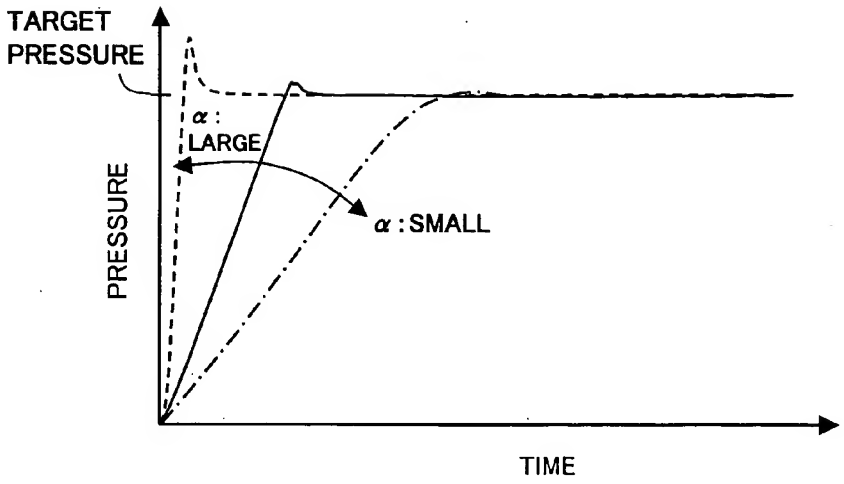
FIG. 6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α:SMALL
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FIG. 7

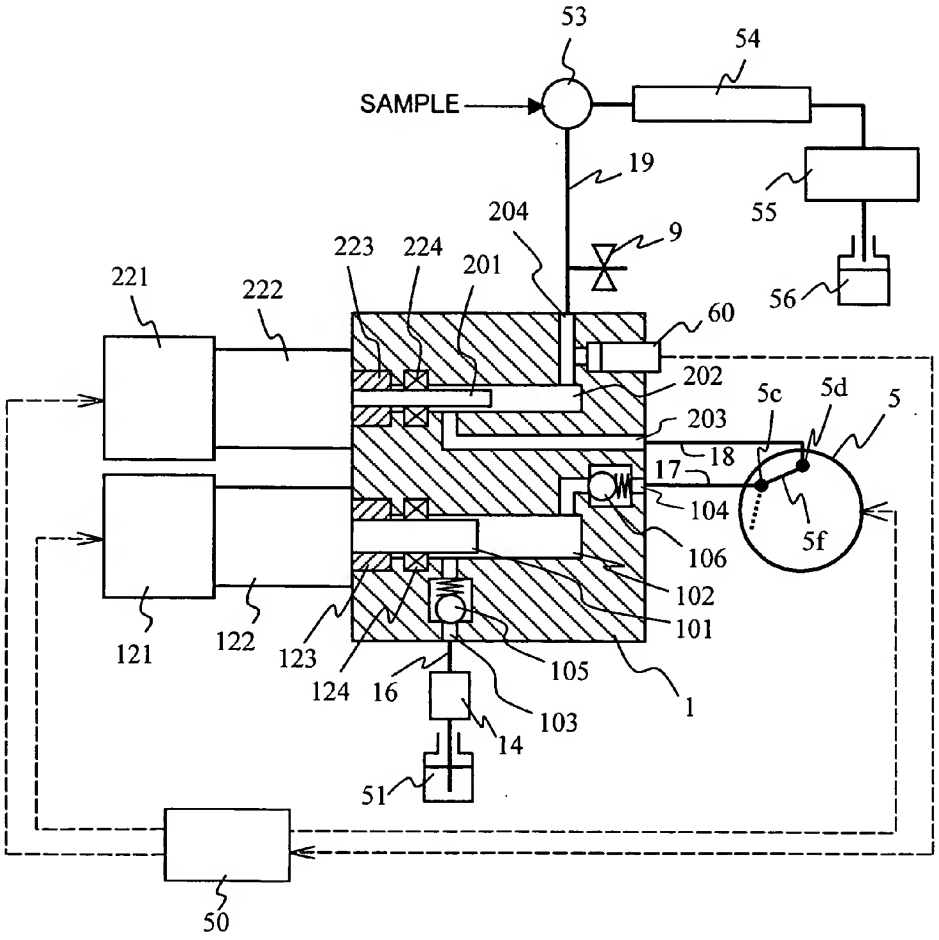
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FIG. 8

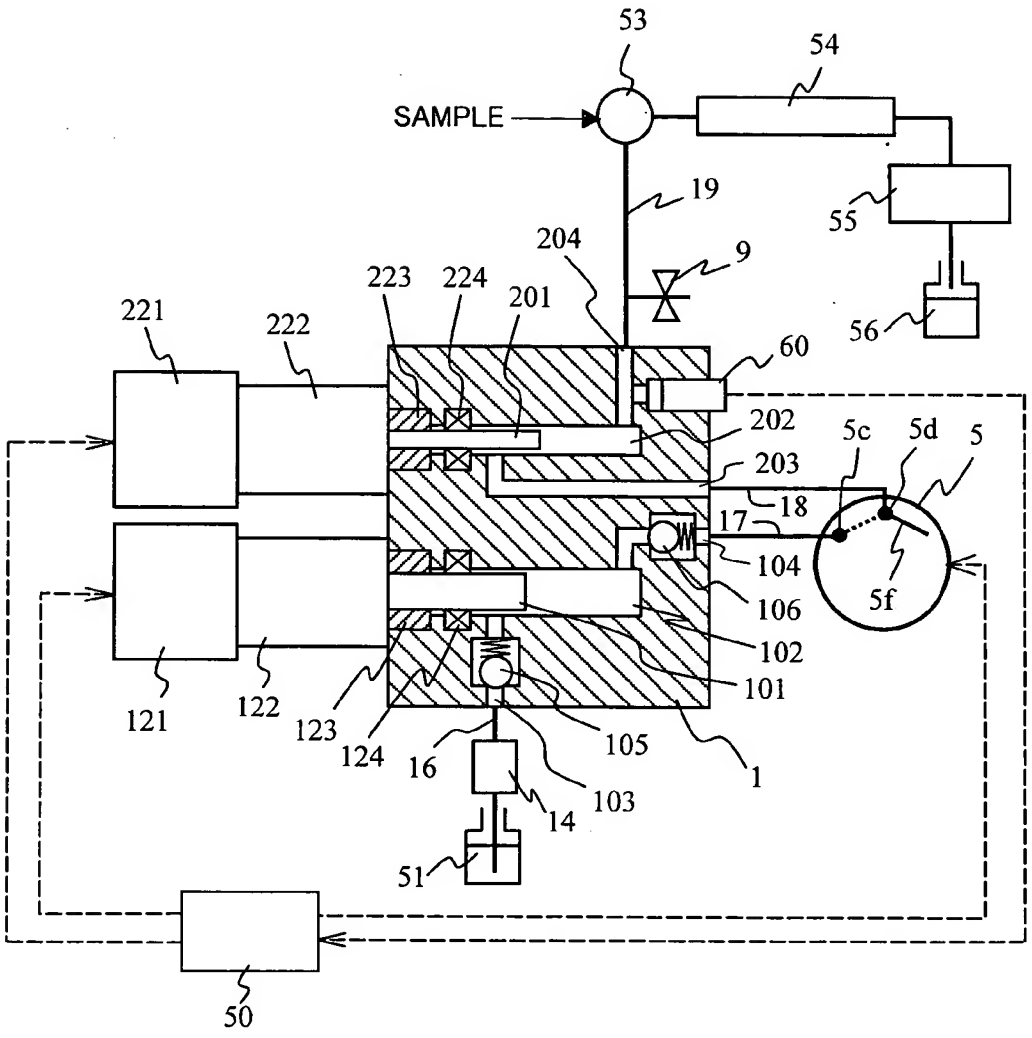
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FIG. 9 A

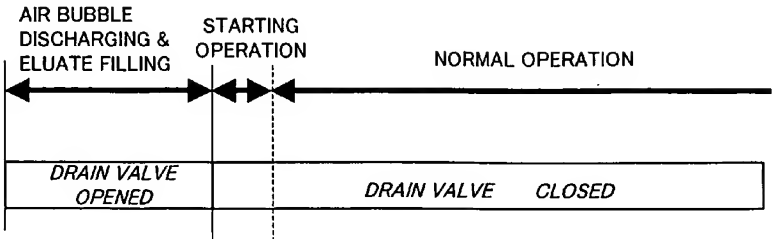

FIG. 9 B

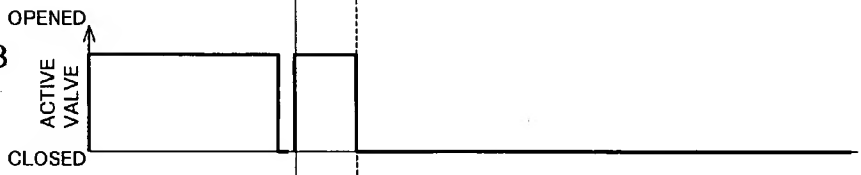

FIG. 9 C

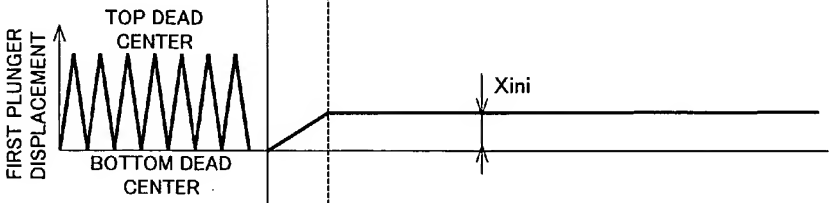

FIG. 9 D

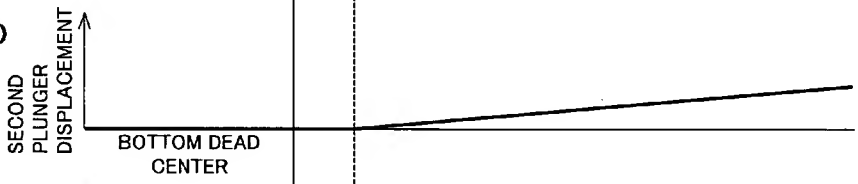

FIG. 9 E

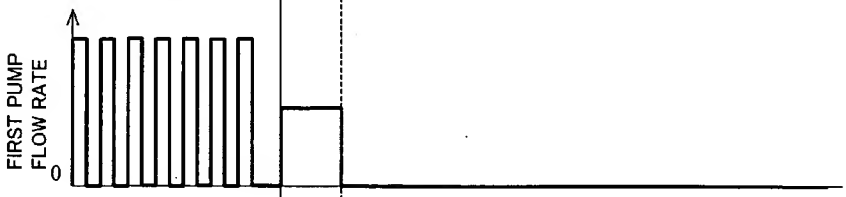

FIG. 9 F

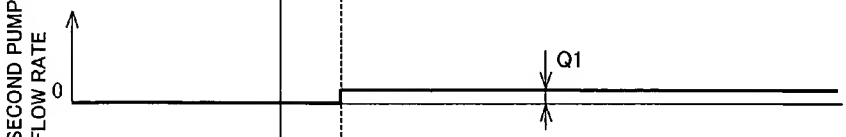

FIG. 9 G

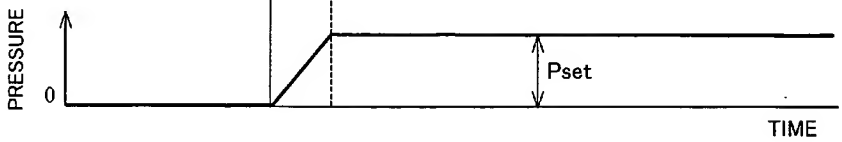

FIG. 10

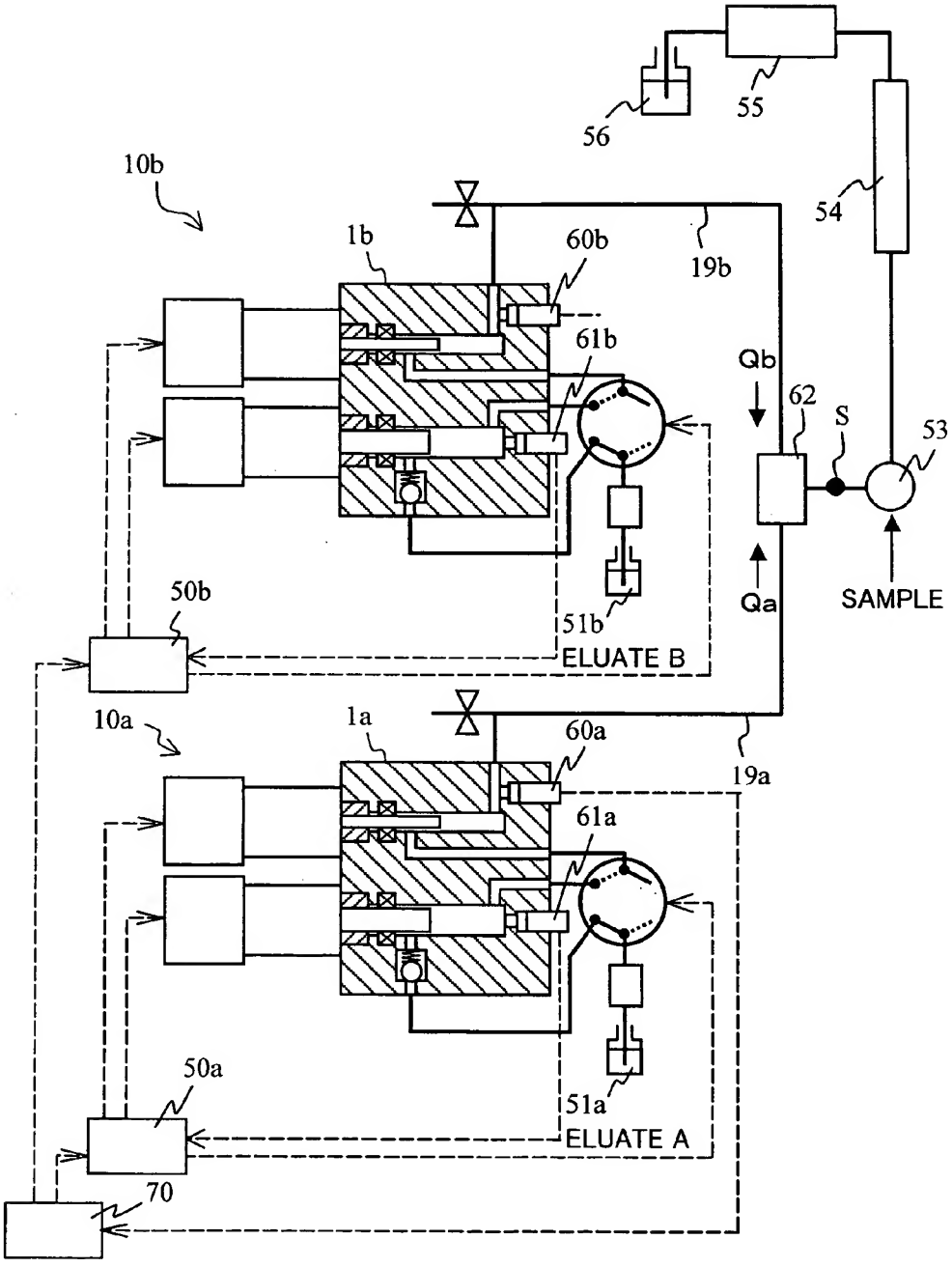
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FIG. 11 A

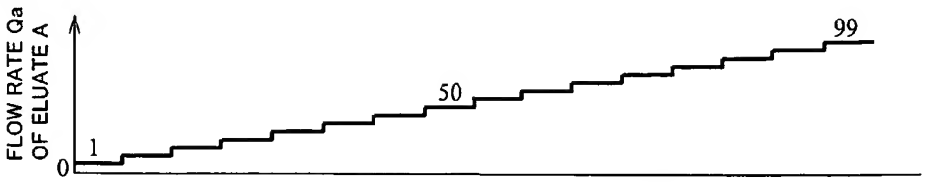


FIG. 11 B

FIG. 11 C

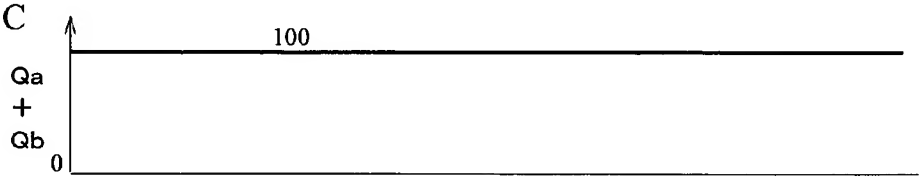


FIG. 11 D

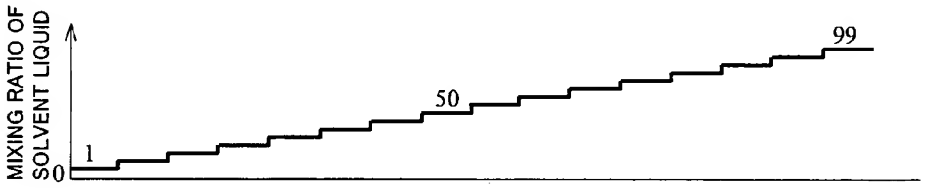


FIG. 11 E

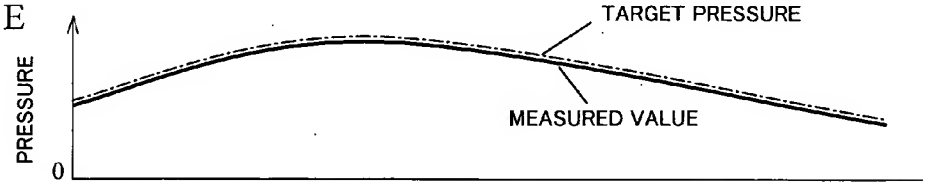


FIG. 11 F

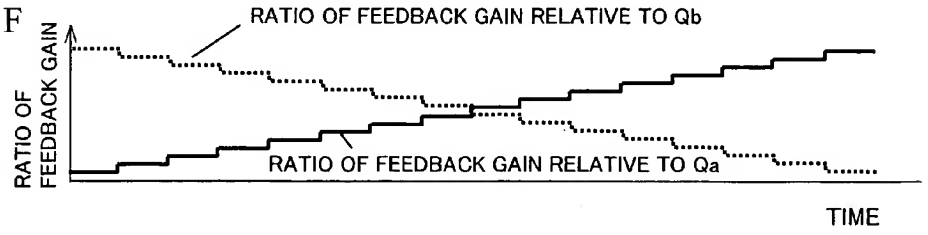
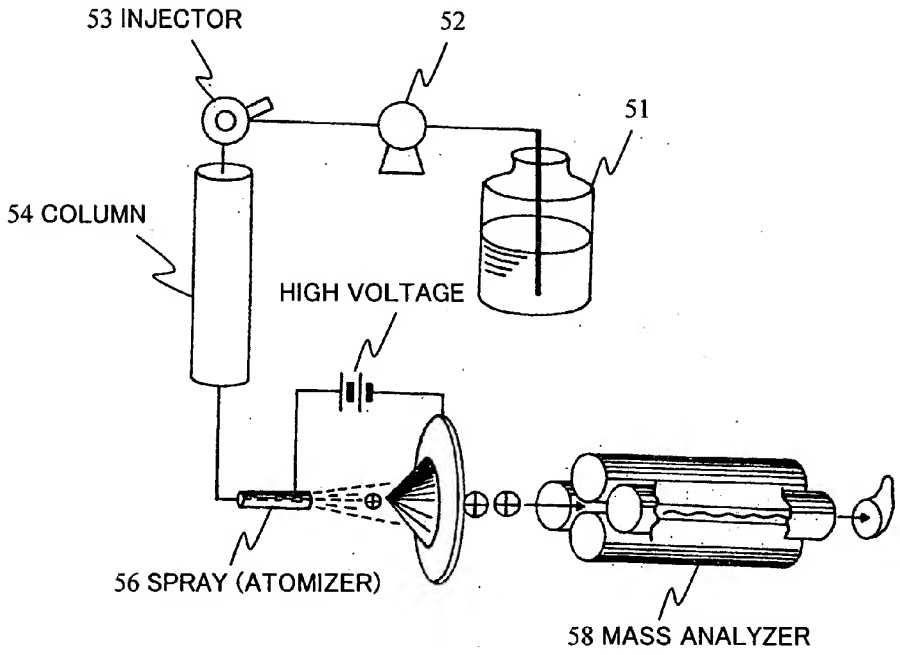


FIG. 12 A



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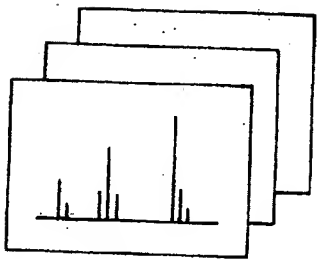


FIG. 12 C

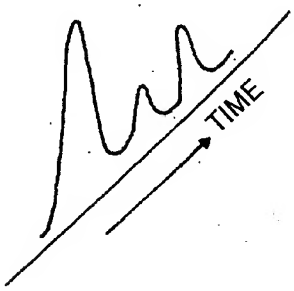
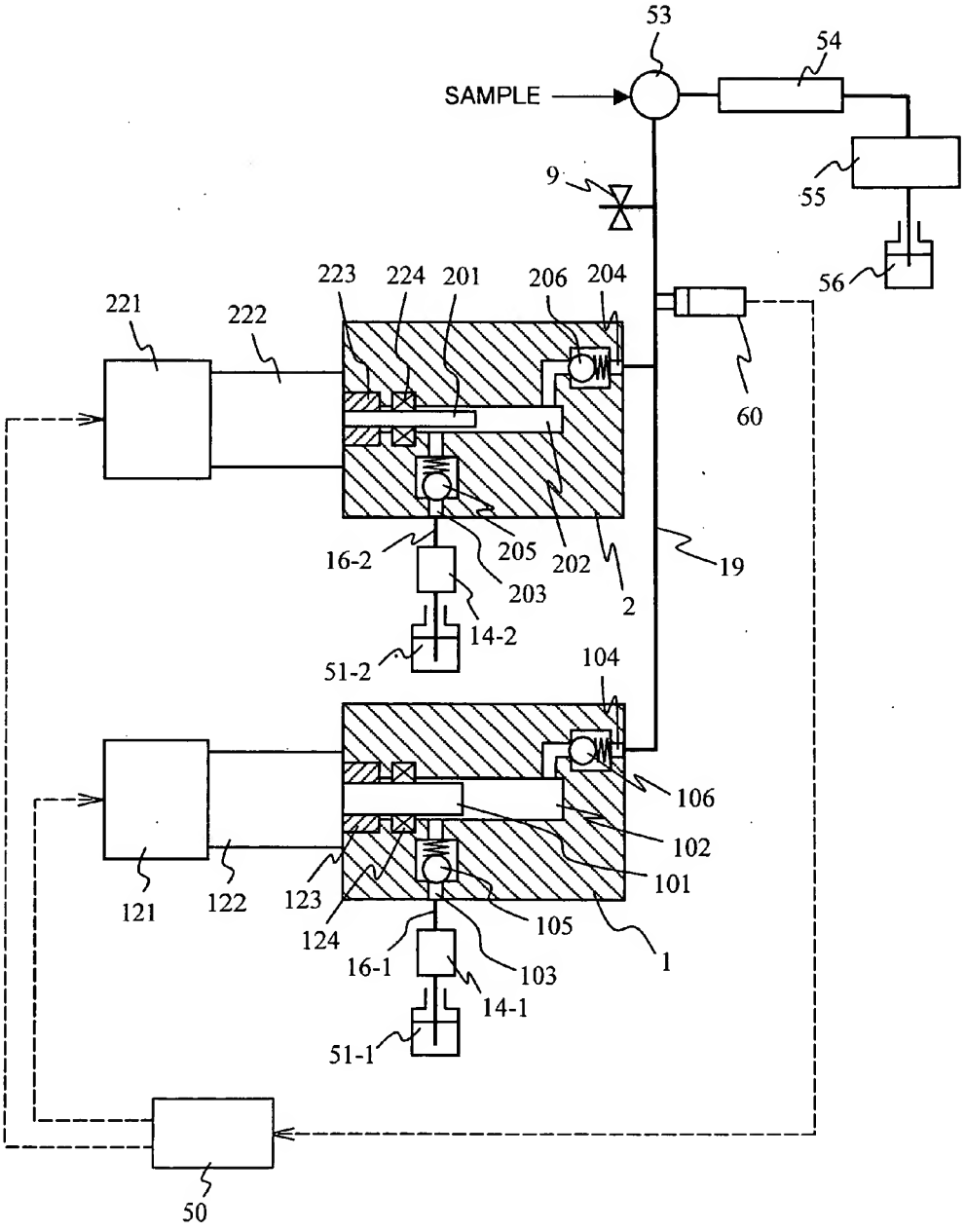


FIG. 13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LIQUID FEEDING SYSTEM

[0001] The present application claims priority from Japanese Application JP2004-195940 filed on Jul. 1, 2004, the content of which is hereby incorporated by reference into this application.

BACKGROUND OF THE INVENTION

[0002] This invention relates to a liquid feeding system suitable for feeding liquid at low flow rate and more particularly to a liquid feeding system which is preferable in its application to a liquid chromatograph.

[0003] As a pump for liquid chromatograph, there has been known in the art to provide a plunger pump having two plungers. In such a plunger pump as above, the two plungers are independently driven with a motor and a pulsation of flow rate is reduced through a cooperative driving of both plungers.

[0004] Example described in the gazette of Japanese Patent Laid-Open No. 75375/1988 shows that a second plunger once performs a reciprocating operation while a first plunger performs a reciprocating operation and then a pulsation in flow rate generated through a sucking operation of the first plunger is corrected through operation of the second plunger. That is, the first plunger determines a liquid feeding flow rate and the second plunger is used for correcting a pulsation of the first plunger.

[0005] Normally, when the pump for a liquid chromatograph is operated, at first, eluate is filled in the pump and a piping to discharge air bubbles. Upon completion of a preparation work performed in this way, subsequently, the pump is activated and the operation is changed over to its normal operation when a discharging pressure reaches a predetermined target value. Upon starting the normal operation, a measurement by the liquid chromatograph is started.

[0006] The pump for liquid chromatograph requires a liquid feeding of low flow rate. For example, it is required to perform a liquid feeding of quite low flow rate under a level of micro-litter (μl) and nano-litter (nl) per minute is required. Either such a pump of low flow rate or a pump of quite low flow rate requires a longer hour after starting a preparation work and by starting of a normal operation. In other words, a starting time at the time of pump energization is extended.

BRIEF SUMMARY OF THE INVENTION

[0007] It is an object of the present invention to reduce a starting time at the time of energization of the pump.

[0008] In order to accomplish the object above, the liquid feeding system of the present invention has the first and second pumps each provided with a plunger. Liquid sucked through the suction port is discharged out of a discharging port through the first and second pumps. Under a starting operation mode, the second pump is stopped and only the first pump is operated. When the discharging pressure at the discharging port reaches a predetermined value, the starting operation mode is changed over to the normal operation mode. Under the normal operation mode, the first pump is stopped and only the second pump is operated. In accordance with the present invention, it is possible to reduce the starting time at the time of starting the pump.

BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING

[0009] FIGS. **1** to **4** are views for illustrating one preferred embodiment of the liquid feeding system of the present invention, wherein **FIGS. 1 and 2** show a block diagram.

[0010] **FIGS. 3 and 4** are views for illustrating a method for driving an active valve.

[0011] **FIGS. 5 and 6** are graphs for illustrating a pressure characteristic of a pump used in a liquid feeding system in **FIG. 1**.

[0012] **FIGS. 7 and 8** are block diagrams for showing another preferred embodiment of the liquid feeding system in accordance with the present invention.

[0013] **FIG. 9** is a view for illustrating a method for driving an active valve used in the system.

[0014] **FIG. 10** is a block diagram for showing one preferred embodiment of the liquid feeding system using a high pressure gradient operating system in accordance with the present invention.

[0015] **FIG. 11** is a view for illustrating its operating method.

[0016] **FIG. 12** is a block diagram for showing one preferred embodiment of a liquid chromatograph and a mass analyzer system using the liquid feeding system of the present invention.

[0017] **FIG. 13** is a block diagram for showing a still further preferred embodiment of the liquid feeding system of the present invention.

DETAILED DESCRIPTION OF THE INVENTION

[0018] Referring now to the drawings, one preferred embodiment of the present invention will be described as follows.

[0019] **FIGS. 1 and 2** illustrate a liquid chromatograph device using the liquid feeding system in accordance with the present invention. The liquid chromatograph device comprises a liquid feeding system, an injector **53**, a column **54**, a detector **55** and a storing tank **56**. The liquid feeding system of the present invention feeds a quite low flow rate of 0.1 nL (nano litter)/min to 50 μL (micron litter)/min, for example, to the column **54**.

[0020] The liquid feeding system of the present preferred embodiment comprises a storing tank **51** for storing eluate or solvent, a deaeration device (degassing unit) **14**, an active valve **5** having four ports, a plunger pump device **1** having two plungers, linear motion mechanisms (actuators) **122**, **222** connected to the plunger, motors **121**, **221** for driving the linear motion mechanisms and a controller **50** for controlling the motors **121**, **221** and the active valve **5**. The active valve **5** is connected to the storing tank **51** through the deaeration device **14** and the suction pipe **15**.

[0021] The plunger pump device **1** is connected to the active valve **5** through the suction pipe **16**, an intermediate discharging pipe **17** and an intermediate suction pipe **18**, and is further connected to the injector **53** through the discharging pipe **19**. The discharging pipe **19** is provided with a drain valve **9**.

[0022] The plunger pump device **1** has a first pressurizing chamber **102** and a second pressurizing chamber **202** and these pressurizing chambers are liquid sealed with seals **124**, **224**. Each of the first plunger **101** and the second plunger **201** is arranged at each of the first pressurizing chamber **102** and the second pressurizing chamber **202**. The first plunger **101** and the second plunger **201** are slidably held by bearings **123**, **223**.

[0023] Both a suction passage **103** and the discharging passage **104** are connected to the first pressurizing chamber **102**. The suction passage **103** is connected to the suction pipe **16**. A suction check valve **105** is arranged at the suction passage **103**. The discharging passage **104** is connected to the intermediate discharging pipe **17**. The suction passage **203** and the discharging passage **204** are connected to the second pressurizing chamber **202**. The discharging passage **204** is connected to the discharging pipe **18**. The discharging passage **204** is connected to the discharging pipe **19**. The discharging passage **204** is provided with a pressure sensor **60**. Further, a pressure in the discharging passage **204** detected by the pressure sensor **60** is defined herein as a pump discharging pressure.

[0024] A segment including the first pressurizing chamber **102**, first plunger **101**, motor **121** for driving the plunger and a linear motion mechanism **122** is defined as a first pump; and another segment including the second pressurizing chamber **202**, second plunger **201**, motor **221** for driving the plunger and a linear motion mechanism **222** is defined herein as a second pump. As shown in the drawings, a diameter of the first plunger **101** is larger than a diameter of the second plunger **201** and accordingly, a flow rate of the first pump is larger than a flow rate of the second pump.

[0025] The active valve **5** is a rotary valve for changing-over a flow passage by an external driving part (not shown) and it has four ports **5***a*, **5***b*, **5***c* and **5***d* and two flow passages **5***e*, **5***f*. Volume of each of the flow passages **5***e*, **5***f* is quite small. The first port **5***a* is connected to the suction pipe **15**, the second port **5***b* is connected to the suction pipe **16**, the third port **5***c* is connected to the intermediate discharging pipe **17** and the fourth port **5***d* is connected to the intermediate suction pipe **18**.

[0026] **FIG. 1** shows a state in which the first port **5***a* and the second port **5***b* are connected by the flow passage **5***e*, although the third port **5***c* and the fourth port **5***d* are not connected to each other. **FIG. 2** shows a state in which the third port **5***c* and the fourth port **5***d* are connected by the flow passage **5***c*, although the first port **5***a* and the second port **5***b* are not connected to each other.

[0027] Rotation of each of the motors **121**, **221** is converted into a linear motion by the linear motion mechanisms **122**, **222** so as to cause each of the first plunger **101** and the second plunger **201** to be reciprocated. The controller **50** gives a driving signal to the motors **121**, **221** in response to a signal of the pressure sensor **60** and at the same time gives a valve opening or closing signal to the active valve **5**.

[0028] Schematic liquid feeding routes at the liquid feeding system in the present preferred embodiment will be described. At first, as shown in **FIG. 1**, when the first port **5***a* and the second port **5***b* are connected by the flow passage **5***e*, solution in the storing tank **51** is guided to the first port **5***a* of the active valve **5** through the deaeration device **14** and the suction pipe **15** and then the solution is guided to the suction passage **103** of the plunger pump device **1** through the first flow passage **5***e*, the second port **5***b* and the suction pipe **16**. The solution is guided to the first pressurizing chamber **102** through the suction check valve **105**.

[0029] In turn, when the third port **5***c* and the fourth port **5***d* are connected by the second flow passage **5***f* as shown in **FIG. 2**, the solution in the first pressurizing chamber **102** is guided to the third port **5***c* of the active valve **5** through the discharging passage **104** and the intermediate discharging pipe **17** and then the solution is guided to the suction passage **203** of the plunger pump device **1** through the second flow passage **5***f*, the fourth port **5***d* and the intermediate suction pipe **18**. Further, the solution is guided to the injector **53** through the second pressurizing chamber **202**, the discharging passage **204** and the discharging pipe **19**.

[0030] Sample to be analyzed is poured through the injector **53**. With such an arrangement as above, the sample is mixed in the solution. The solution containing the sample is fed into the column **54** and the constituents contained in the sample are separated from each other. Each of the separated constituents is analyzed by the detector **55**. Some fine silica gel particles are already filled in the column **54** and then a load pressure of about 10 MPa is generated at the plunger pump device **1** through a fluid resistance when the solution flows there. A value of the load pressure is changed in response to a diameter of the column and its passing flow rate.

[0031] Referring to **FIG. 3**, an operation of the liquid feeding system of the present preferred embodiment will be described. Concurrently, **FIGS. 1 and 2** are also referred to. **FIG. 3A** shows a drain valve opening or closing operation, **FIG. 3B** shows an opening or closing operation of the active valve **5** in respect to the first plunger **101**, **FIG. 3C** shows a displacement of the first plunger **101**, **FIG. 3D** shows an opening or closing operation of the active valve **5** in respect to the second plunger **201**, **FIG. 3E** shows a displacement of the second plunger **201**, **FIG. 3F** shows a first pump flow rate, **FIG. 3G** shows a second pump flow rate and **FIG. 3H** shows a discharging pressure of the pump detected by the pressure sensor **60**. An X-axis denotes a time.

[0032] In addition, as shown in the sample of **FIG. 1**, a state in the active valve **5** in which the first port **5***a* and the second port **5***b* are connected by the flow passage **5***e* and the third port **5***c* and the fourth port **5***d* are not connected is defined as "opened" in respect to the first plunger **101** and is also defined as "closed" in respect to the second plunger **201**. At this time, the first pressurizing chamber **102** is connected to the solution in the storing tank **51** via the active valve **5**, but is not connected to the second pressurizing chamber **202**.

[0033] As shown in **FIG. 2**, the state that the third port **5***c* and the fourth port **5***d* are connected by means of the flow passage **5***f*, and the first port **5***a* and the second port **5***b* are not connected thereby, is defined as "closed" for the first plunger **101**, and is defined as "opened" for the second plunger **201**. Then, the first pressurizing chamber **102** is connected to the second pressurizing chamber **202** via the active valve **5**; but is not connected to the solution in the storing tank **51**. When the active valve **5** is opened to the first plunger **101**, it is closed to the second plunger **201**. Inversely, when the valve is closed to the first plunger **101**, it is opened to the second plunger **201**.

[0034] Further, the first plunger **101** and the second plunger **201** are defined such that a state in which they are pulled in by the motors **121**, **221** and the linear motion mechanisms **122**, **222**, i.e. they are arranged at the left end of the pressurizing chamber in **FIGS. 1 and 2** is defined as being set at a bottom dead center and in turn a state in which they are pushed in by the motor **21** and the linear motion mechanism **22**, i.e. they are arranged at the right end of the pressurizing chamber in **FIGS. 1 and 2** is defined as being set at a top dead center.

[0035] Under the eluate filling and air bubble discharging mode before starting test in the preferred embodiment, the first pump and the second pump are used, and under the starting operation mode, the first pump is used and when a quite low flow rate liquid feeding under the normal operation mode is to be carried out, the second pump is used.

[0036] At first, the air bubble discharging and eluate filling mode will be described. Under the air bubble discharging and eluate filling mode, the air bubbles in the pump, passage and pipe contained in the liquid feeding system of the preferred embodiment are discharged out and then the eluate is filled. As shown in **FIG. 3A**, the drain valve **9** is released. Comparing **FIGS. 3B and 3D** to each other shows that an opening or closing operation of the active valve **5** for the second plunger **201** is delayed by a semi-period relative to the opening or closing operation for the first plunger.

[0037] Comparing **FIGS. 3C and 3E** to each other shows that when the first pump is in the suction stroke, the second pump is in the discharging stroke. Inversely, when the first pump is in the discharging stroke, the second pump is in the suction stroke.

[0038] Comparing **FIGS. 3B through 3E** shows that a reciprocating motion of the second plunger **201** is delayed by a semi-period relative to the reciprocating motion of the first plunger **101**. When the first plunger **101** is moved from its drawn top dead center to its bottom dead center, the second plunger **201** is pushed in and moved from the bottom dead center to the top dead center. That is, the suction stroke at the first pump becomes a discharging stroke at the second pump. In turn, when the first plunger **101** is pushed in and moved from the bottom dead center to the top dead center, the second plunger **201** is drawn into and moved from the top dead center to the bottom dead center. That is, the discharging stroke at the first pump becomes the suction stroke at the second pump.

[0039] Comparing **FIGS. 3F and 3G** to each other shows that operations of the first plunger and the second plunger **2** are delayed in period by ¼ in respect to the opening or closing operation of the active valve **5**. Accordingly, each of the opening or closing operation of the active valve **5** in **FIG. 3B** in respect to the first plunger **101**, the reciprocating motion of the first plunger **101** in **FIG. 3C**, the opening or closing operation of the active valve **5** in respect to the second plunger **2** in **FIG. 3D** and the reciprocating motion of the second plunger **2** in **FIG. 3E** is delayed in sequence in a period by ¼, respectively.

[0040] For example, as shown in **FIG. 3B**, the active valve **5** is changed from the "closed" state to the "opened" state in respect to the first plunger **101**. Next, as shown in **FIG. 3C**, the first plunger **101** is changed from the top dead center to the bottom dead center with a delay of period by ¼ to perform the suction stroke of the first pump. Next, as shown in **FIG. 3D**, the active valve **5** is changed from the "closed" state to the "opened" state in respect to the second plunger **2** with a delay of period by ¼. Next, as shown in **FIG. 3E**, the second plunger **2** is changed from the top dead center to the bottom dead center with a delay of period by ¼ to perform the suction stroke of the second pump.

[0041] As shown in **FIG. 3B**, the active valve **5** is changed from the "opened" state to the "closed" state in respect to the first plunger **101** with a delay of half-period. Then, as shown in **FIG. 3C**, the first plunger **101** is changed from the bottom dead center to the top dead center with a delay of period by ¼ to perform the discharging stroke of the first pump. Next, as shown in **FIG. 3D**, the active valve **5** is changed from the "opened" state to the "closed" state in respect to the second plunger **2** with a delay of period by ¼. Next, as shown in **FIG. 3E**, the second plunger **2** is changed from the bottom dead center to the top dead center with a delay of period by ¼ to perform the discharging stroke of the second pump.

[0042] As shown in **FIG. 3H**, although the discharging pressures of the pumps include varying components of the first pump flowing rate and the second pump flowing rate, they become substantially constant.

[0043] As shown in **FIG. 3**, the first plunger and the second plunger are reciprocated by several times under the air bubble discharging and eluate filling mode. A difference volume between the first pump flowing rate and the second pump flowing rate is discharged out of the drain valve **9** and simultaneously the air bubbles are also removed. In the present preferred embodiment, since the upstream side first pump has a high flowing rate, it is possible to perform an easy discharging of air bubbles accumulated in the second downstream side pressurizing chamber **202**. With this operation, a test preparation can be completed in a shorter time.

[0044] Upon completion of the air bubble discharging and eluate filling mode, the first and second plungers and the active valve are arranged at their home positions described later.

[0045] Next, an operation in which the pump starting operation is transferred to the normal operation will be described as follows. The first and second plungers and the active valve are arranged at their home positions. At the home position, the active valve **5** is "opened" in respect to the first plunger **101** and "closed" in respect to the second plunger **201**. In addition, the first and second plungers are arranged at the bottom dead center. Accordingly, eluate is filled in the first and second pressurizing chambers.

[0046] Subsequently, when the active valve **5** is "opened" in respect to the first plunger **101**, it is merely described that the active valve **5** is "opened". Accordingly, a state in which the active valve **5** is "opened" is meant that it is "opened" in respect to the first plunger **101** and it is "closed" in respect to the second plunger **201** as shown in **FIG. 1**. When the active valve **5** is "closed" in respect to the first plunger **101**, it is merely described that the active valve **5** is "closed". Accordingly, a state in which the active valve **5** is "closed" means that it is "closed" in respect to the first plunger **101** and it is "opened" in respect to the second plunger **201** as shown in **FIG. 2**.

[0047] When the active valve **5** is placed at the home position, it is "opened". At first, the drain valve **9** is closed

as shown in **FIG. 3A** and the active valve **5** is changed from the "opened" state to the "closed" state as shown in **FIG. 3B** and **FIG. 3D**. Accordingly, as shown in **FIG. 2**, the first pressurizing chamber **102** is connected to the second pressurizing chamber **202** through the active valve **5**. As shown in **FIG. 3C**, the first plunger **101** is moved from the bottom dead center toward the top dead center at a predetermined speed and the discharging stroke of the first pump is carried out. As apparent from the gradient in the graph, the moving speed of the first plunger **101** at the starting operation of the pump is slower than that of the air bubble discharging and eluate filling mode. As shown in **FIG. 3E**, the eluate discharged out of the first pressurizing chamber **102** is guided to the second pressurizing chamber **202** through the active valve **5** and from there, the eluate is discharged to the discharging pipe **19**. At this time, the second pump is not substantially operated. Accordingly, although the flow rate of the first pump becomes a predetermined value corresponding to the moving speed of the first plunger **101**, the flow rate of the second pump is zero as shown in **FIG. 3G**.

[**0048**] When the discharging pressure of the pump reaches up to the target pressure Pset as shown in **FIG. 3H**, the operation is changed over to the normal operation. The target pressure Pset is determined in response to a diameter of the column and a passing flow rate. When the discharging pressure of the pump reaches up to the target pressure Pset, the pressure sensor **60** informs it to the controller **50**.

[**0049**] The controller **50** transmits a command under the normal operation mode to the first and second pumps and the active valve **5**. Under the normal operation, a liquid feeding flow rate is kept constant while holding the discharging pressure to the target pressure Pset.

[**0050**] Under the normal operation, the active valve **5** us changed from the "closed" state to the "opened" state as shown in **FIG. 3B** and FIG. **3**D. Accordingly, the second pressurizing chamber **202** is shut by the first pressurizing chamber **102** as shown in **FIG. 1**. The first plunger **101** is stopped as shown in **FIG. 3C**. The first plunger **101** is arranged at a predetermined position between the bottom dead center and the top dead center. Next, the second plunger **201** is moved from the bottom dead center toward the top dead center at a slow speed as shown in **FIG. 3E**. The discharging stroke of the second pump is executed at a slow speed. The flow rate of the first pump becomes zero as shown in **FIG. 3F** and a flow rate of the second pump becomes a target flow rate Qset as shown in **FIG. 3G**. In this example, the second plunger **201** is pushed in at a constant slow speed, thereby the discharging pressure is held at the target pressure Pset and the liquid feeding flow rate can be held at the target flow rate Qset.

[**0051**] When the normal operation is carried out in this way, the sample of the item to be analyzed is poured by the injector **53**, the mixed solution enters into the column **54**, they are separated for every constituent and then the constituents are analyzed by the detector **55**.

[**0052**] In this example, only the first pump is operated under the pump starting operation and only the second pump is operated under the normal operation. Under this operating method, it is possible to shorten the reaching time up to the target pressure, i.e. the starting time of the pump starting time.

[**0053**] Next, a changing-over operation for changing-over from the starting operation to the normal operation will be described as follows. Practically, there occurs sometimes that the pump pressure shows an over-shoot from the target pressure Pset and a starting time is extended due to a reply time at the time of changing-over of the active valve **5** or a presence of the dead volume of the active valve **5**. Then, its counter-measure will be described as follows.

[**0054**] **FIG. 4** illustrates another operating method for the liquid feeding system of the present invention in the same way as that shown in **FIG. 3**. Description of both discharging of air bubbles and filling of the eluate will be omitted because they are similar to those shown in **FIG. 3**.

[**0055**] In this example, only the first pump is operated under the starting operation of the pump in the same manner as that of the example in **FIG. 3**. When the pump discharging pressure reaches up to a value (Pset−ΔPset) lower only by ΔPset as shown in **FIG. 4H**, the operation is changed over to the normal operation. Upon starting of the normal operation, the active valve **5** is changed from its "closed" state to its "opened" state as shown in **FIG. 4B** and **FIG. 4D**. As shown in **FIG. 4C**, the first plunger **101** is stopped. The first pump flow rate becomes zero as shown in **FIG. 4F** and the second pump flow rate becomes a target flow rate Qset as shown in **FIG. 4G**. The pump discharging pressure is increased and reaches up to the target pressure Pset as shown in **FIG. 4H**.

[**0056**] In this example, it is possible to reduce the over-shoot from the target pressure by performing it with changing-over time from the first plunger **101** to the second plunger **201** being faster only by Δt as compared with the operating method shown in **FIG. 3**. Further, a gradient of the pump discharging pressure at the time Δt is smaller than a gradient of the pump discharging pressure at the starting operation.

[**0057**] Further, although the plunger changing-over time is adjusted for reducing the over-shoot in this example, it may also be applicable to employ another method, a method for reducing a feeding speed of the first plunger **101**, for example. In this way, an operation for adjusting the plunger changing-over time or reducing the feeding speed of the first plunger **101** to reduce the over-shoot is defined as a pressure correction hereinbelow.

[**0058**] Then, referring to **FIG. 5** and **FIG. 6**, an effect of the present preferred embodiment will be described.

[**0059**] **FIG. 5** shows a result of variation in the pump discharging pressure when an operation of the pump is changed from the starting operation to the normal operation. A solid line curved line **501** in **FIG. 5** indicates a pump discharging pressure when the pressure correction is performed and a dotted curved line **502** indicates a pump discharging pressure when the pressure correction is not performed.

[**0060**] When the pressure correction is not carried out, the pump starting time is extended and at the same time a disturbance of the starting time is increased. To the contrary, when the pressure correction is carried out, the pump starting time is substantially shortened and at the same time a disturbance in the starting time is almost eliminated. Further, although not shown in the drawing, when the pressure correction is not carried out, a case when the pressure does not reach up to the target pressure in correspondence with either the target flow rate or target pressure

of the second pump was generated and such a phenomenon was not generated when the pressure correction was carried out.

[0061] Referring to **FIG. 6**, when a pressure correction is carried out by the first pump (operation of the first plunger), a flow rate relation between the first pump and the second pump will be described. A following equation of

$$Q1=\alpha Q2 \quad \text{(Ex. 1)}$$

can be attained, where Q1 is a first pump set flow rate (a value in which a sectional area of the first plunger is multiplied by a feeding speed of the first plunger), Q2 is a second pump set flow rate (a value in which a sectional area of the second plunger is multiplied by a feeding speed of the first plunger) and α is a coefficient of flow rate at that time.

[0062] **FIG. 6** shows a relation between the coefficient α of flow rate and a pump starting characteristic. Although the higher the coefficient α of flow rate, the shorter the pump starting characteristic, too higher coefficient value causes an over-shoot to be generated. To the contrary, although the smaller the coefficient α of flow rate, the longer a pump starting time, no over-shoot may be generated. The coefficient α of flow rate=1 corresponds to the case in which the first pump set flow rate is the same as the second pump set flow rate. When the coefficient α of flow rate=1 is applied, there may occur a case in which the pump pressure does not reach up to the target pressure. Accordingly, the coefficient α of flow rate is at least larger than 1.

[0063] As the coefficient α of flow rate, the most-suitable value is present. The most-suitable value of the coefficient α of flow rate may be different in compliance with the target pressure and the target flow rate. In other words, if the target pressure and the target flow rate are determined, the most-suitable value of the coefficient α of flow rate can be attained. When an analysis is carried out with a liquid chromatograph using the liquid feeding system of the present invention, for example, it is preferable to make a map in advance for the target pressure in respect to the target flow rate. It is also possible to perform an automatic starting-up of the liquid feeding system of this example through utilization of this map. For example, a user inputs the target pressure. The liquid feeding system reads the target flow rate corresponding to the target pressure from the map and gets the most-suitable value of the coefficient α of flow rate from the target flow rate. In this way, the most-suitable value of the coefficient α of flow rate is applied as an input value and the liquid feeding system is operated.

[0064] In the examples shown in **FIG. 1** and **FIG. 2**, although a diameter of the first plunger is constituted to be larger than a diameter of the second plunger, it may also be applicable that the first plunger diameter and the second plunger diameter are made same to each other to cause the moving speed of the first plunger to be larger than the moving speed of the second plunger. With this arrangement above, the first pump flow rate becomes larger than the second pump flow rate.

[0065] Referring to FIGS. **7** to **9**, another example of the liquid feeding system of the present invention will be described. Same reference symbols are applied to the same portions as those of the first example in the liquid feeding system shown in FIGS. **1** to **3**, and their description will be properly eliminated. In this example, the active valve **5** has two ports Sc, **5***d* and one flow passage **5***f*.

[0066] The first port **5***c* of the active valve **5** is connected to the discharging passage **104** of the first pump and the second port **5***d* is connected to the suction passage **203** of the second pump. The suction passage **103** of the first pump is connected to the storing tank **51** through a deaeration device **14** and the suction pipe **16**. The discharging passage **104** of the first pump is provided with a discharging check valve **106**. The first pump flow rate is larger than the second pump flow rate in the same manner as that of the first example.

[0067] **FIG. 7** shows a state in which the first and second ports **5***c*, **5***d* of the active valve **5** are connected to each other by the flow passage Sf. In this case, this state is defined that the active valve **5** is "opened". **FIG. 8** shows a state in which the first and second ports **5***c*, **5***d* of the active valve **5** are not connected to each other. In this case, this state is defined that the active valve **5** is "closed".

[0068] Referring to **FIG. 9**, a method for operating the liquid feeding system in this example will be described. At first, the air bubble discharging and eluate filling mode will be described. The drain valve **9** is "opened" as shown in **FIG. 9A** and the active valve **5** is "opened" as shown in **FIG. 9B**. The first plunger **101** is reciprocated at a fast speed as shown in **FIG. 9C**. At this time, the second plunger is arranged at the bottom dead center as shown in **FIG. 9D**. As shown in **FIG. 9E**, liquid is fed by an upstream side first pump having a high flow rate, the air bubbles in the first and second pumps are discharged and eluate is filled. The downstream side second pump flow rate having a small flow rate is zero. As shown in **FIG. 9G**, the pump discharging pressure is zero.

[0069] In this example, it is possible to perform an easy discharging of the air bubbles accumulated in the downstream side second pressurizing chamber because the air bubble discharging and eluate filling mode is carried out by the upstream side first pump having a higher capacity. With such an arrangement as above, it is possible to complete a test preparation within a shorter time. Although a flow rate of the pump is set intermittently as shown in **FIG. 9E**, a pulsation in flow rate under this mode does not provide any influence on a measurement precision, so that no problem occurs.

[0070] Next, changing-over in operation from the starting operation to the normal operation will be described. Under the pump starting operation, the drain valve **9** is "closed" as shown in **FIG. 9A** and the active valve **5** is kept at the "opened" state as shown in **FIG. 9B**. As shown in **FIG. 9C**, the first plunger **101** is moved from the bottom dead center toward the top dead center at a predetermined speed. At this time, the second plunger is arranged at the bottom dead center as shown in **FIG. 9D**. As shown in **FIG. 9E**, the first pump flow rate becomes a predetermined value in compliance with the moving speed of the first plunger **101**. As shown in **FIG. 9F**, the second pump flow rate is zero. As shown in **FIG. 9G**, the pump discharging pressure is increased. When the pump discharging pressure reaches up to the target pressure Pset, the operation is changed over to the normal operation. In this example, when the position of the first plunger **101** became Xini, the pump discharging pressure reached up to the target pressure Pset.

[0071] Under the normal operation, the active valve **5** is "closed" as shown in **FIG. 9B**. The position of the first

plunger **101** is held at Xini as shown in **FIG. 9C** and the second plunger **201** is pushed into the second pressurizing chamber **202** at a slow speed as shown in **FIG. 9D**. At this time, as shown in **FIG. 9E**, the first pump flow rate is zero and as shown in **FIG. 9F**, the second pump flow rate becomes the target flow rate Q1.

[0072] As described above, in accordance wit the liquid feeding system of this example, there is provided an effect capable of performing the air bubble discharging and eluate filling within a short period of time and improving a durability of the active valve because the changing-over times of the active valve can be reduced.

[0073] **FIG. 10** shows an example of a high pressure gradient operation system. The high pressure gradient operation system has two liquid feeding systems connected to each other to perform a high pressure gradient operation. The high pressure gradient operation system of this example includes two liquid feeding systems **10***a*, **10***b*, main controller **70** and mixer **62**. The second pump discharging passages in the two liquid feeding systems **10***a*, **10***b* are provided with each of the first pressure sensors **60***a*, **60***b*, and the first pressurizing chamber is provided with each of the second pressure sensors **61***a*, **61***b*. The two liquid feeding systems **10***a*, **10***b* are the same as the liquid feeding system shown in **FIG. 1** except the fact that there are provided second pressure sensors **61***a*, **61***b*. Each of the two liquid feeding systems **10***a*, **10***b* may be the aforesaid other liquid feeding systems in place of the liquid feeding system in **FIG. 1**.

[0074] Discharging pipes **19***a*, **19***b* of the two liquid feeding systems **10***a*, **10***b* are connected to the mixer **62**. The discharging side of the mixer **62** is connected to the injector **53**.

[0075] Referring to **FIG. 11**, the gradient operation will be described. The gradient operation is meant to feed liquid while a mixing ratio of the two kinds of eluate A and B is being changed in a stepwise manner as time passes by. That is, a ratio between the two liquid feeding flow rates Qa and Qb is changed while a total liquid feeding flow rate (Qt=Qa+Qb) is being kept constant. As shown in **FIG. 11A**, the flow rate Qa of the first eluate A is increased in a stepwise manner as time passes by and it is changed in a stepwise manner from Qa=1 to Qa=99, for example. As shown in **FIG. 11B**, a flow rate Qb of the second eluate B is decreased in a stepwise manner as time passes by, and this is changed in a stepwise manner from Qb=99 to Qb=1, for example. As shown in **FIG. 11C**, a total liquid feeding flow rate Qt=Qa+Qb is kept constant and its value is assumed to be 100. Further, the total liquid feeding flow rate Qt is a flow rate of the mixer **62**. **FIG. 11D** shows a mixing ratio of solutions at the discharging point S of the mixer **62**. A mixing ratio between the first eluate A and the second eluate B is increased in a stepwise manner as time passes by. It is changed in a stepwise manner from Qb/Qa=1 to Qb/Qa=99, for example. This example is a gradient in 100 steps. Accordingly, when the total liquid feeding flow rate Qt is defined as 1 μL/min, a minimum flow rate and resolution are 1/100, i.e. 10 nL/min.

[0076] **FIG. 11E** shows a pump discharging pressure. Two pump discharging pipes **19***a*, **19***b* are connected through the mixer **62**. Ignoring either a pressure reduction or a pressure loss caused by the mixer **62** shows that the two pump discharging pressures are the same to each other. That is, the discharging pressure detected by the first pressure sensor **60***a* of the first pump is equal to the discharging pressure detected by the second pressure sensor **60***b* of the second pump. Further, the discharging pressures detected by these pressure sensors **60***a*, **60***b* are equal to the discharging pressure of the mixer **62**.

[0077] As shown in **FIG. 11C**, even if the total liquid feeding flow rate Qt is kept constant, the pump discharging pressure is changed by about a maximum of 1.5 to 2 times as shown in **FIG. 11E**. This is due to the fact that when the mixing ratio between the two eluates is changed, a fluid resistance when they pass through the column is changed. When it is tried to keep the pump discharging pressure constant, in turn, the total liquid feeding flow rate Qt does not become constant.

[0078] In turn, a relation between the mixing ratio and the pressure variation is already known in reference to the past experimental data. Accordingly, a pressure variation curve when the total liquid feeding flow rate Qt is kept constant can be estimated. Thus, the discharging pressure of the mixer **62** is measured, the measured value is compared with the estimated value at the pressure variation curve and the pump may be driven with a deviation between both values being applied as a feed-back signal.

[0079] A solid curve in **FIG. 11E** shows measured values of the pump discharging pressure and a dotted line curve shows target pressures attained by the past experimental data.

[0080] As shown in **FIG. 10**, an output from the first pressure sensor **60***a* arranged at the pump in the first liquid feeding system is fed back to the main controller **70**. The main controller **70** compares the measured value from the first pressure sensor **60***a* with the target pressure to attain a deviation between them. This deviation is transmitted to each of the pump controllers **50***a*, **50***b*. The controllers **50***a*, **50***b* control each of the pumps in response to the deviation.

[0081] When the pump discharging pressure is lower than the target pressure, the total liquid feeding flow rate (Qt=Qa+Qb) is reduced. Accordingly, it is satisfactory that the total liquid feeding flow rate is increased. However, it is vague which one of the two liquid feeding flow rates Qa and Qb is reduced more. When it is erroneously judged that the second liquid feeding flow rate Qb is reduced even if actually the first liquid feeding flow rate Qa is reduced and the second liquid feeding flow rate Qb is increased, a precision of the mixing ratio is deteriorated. This is a problem called as a mutual interference at the gradient operation.

[0082] In this example, it is assumed that two liquid feeding flow rates Qa and Qb are increased or decreased under the same rate. Accordingly, as shown in **FIG. 11F**, a feed-back gain proportional to the flow rate ratio is given in respect to the two liquid feeding flow rates Qa and Qb. That is, it performs a proportional control. When the ratio of the two liquid feeding flow rates Qa:Qb is 20:80, for example, a feed-back gain of the two liquid feeding flow rates Qa and Qb is given by (20/100)×K and (80/100)×K, respectively. K is a constant. When the total liquid feeding flow rate Qt is lack only by 5, each of the instruction values for the pump is given by **20**+(20/100)×K×5 and 80+(80/100)×K×5, respectively. When K is 1, for example, the former becomes

21 and the latter becomes 84. Although applying this method cannot avoid any reduction in precision of mixing ratio due to a respective difference between the two pumps, mutual interference can be avoided.

[0083] With the foregoing arrangement, it is possible to improve a liquid feeding stability and mixing precision in the high pressure gradient system.

[0084] **FIG. 12**(*a*) shows an example in which a liquid chromatograph and a mass analyzing system are constituted through application of the liquid feeding system of the present invention. The liquid chromatograph includes a liquid feeding system **52**, injector **53**, column **54** and high voltage spray (atomizer) **56**. In this example, as an interface connecting the liquid chromatograph with the mass analyzer **58**, an electro-spray ionization (ESI) process used for analyzing substances having a high polarity such as protein or peptide and the like is applied. In the electro-spray ionization process, when sample solution is fed into a capillary tube applied with a high voltage of about 3 to 5 kV, quite fine spray (atomization) is generated under an atmospheric pressure and then the sample molecules are ionized. In this way, the ionized sample molecules are fed into the mass analyzer. The mass analyzer analyzes a value in which the mass is divided by an electrical charge and specifies its molecular weight.

[0085] **FIG. 12**(*b*) and **FIG. 12**(*c*) show one example of processing data at the mass analyzer. **FIG. 12**(*b*) shows a mass spectrum and **FIG. 12**(*c*) shows a mass chromatogram.

[0086] Although protein is extracted from the collected cells and analyzed in the proteome analysis, a volume of the protein contained in the cells is ultra-fine volume and its growing is also impossible. Accordingly, it is necessary to attain a low flow rate at the liquid chromatograph so as to increase a sensing precision at the liquid chromatograph and the mass analyzer system. In addition, it takes several hours as the analyzing time starting from feeding of sample to data processing.

[0087] It is possible to attain a fine amount of analytical sample fed into the liquid chromatograph by applying the liquid feeding system of the present invention to the liquid chromatograph and the mass analyzer system described above. In addition, it is possible to assure the analyzing time of longer hours because the starting time at the pump starting time is short in the liquid feeding system of the present invention. As a result, it is possible to increase the number of processing of data. In addition, when the pump pressure is monitored and reaches up to a predetermined value (the aforesaid target pressure, for example), it may also be applicable that the sample is fed and its analysis is started. With this operation, a power-saving can be accomplished.

[0088] **FIG. 13** shows another example of the liquid feeding system of the present invention. Same reference symbols are applied to the same portions in the liquid feeding system in **FIG. 1** and their description will be properly eliminated. The feature of this example consists in the fact that the first pump and the second pump are constituted as separate pumps. The liquid feeding system in this example has two storing tanks **51-1**, **51-2**, two deaeration devices (de-gassing units) **14-1**, **14-2**, two plunger pump devices **1**, **2**, linear motion mechanisms (actuators) **122**, **222**, motors **121**, **221** for driving the linear motion mechanisms and controller **50**.

[0089] The two plunger pump devices **1**, **2** are connected to the injector **53** through the discharging pipe **19**. The discharging pipe **19** is provided with the drain valve **9** and the pressure sensor **60**. Each of the two plunger pump devices **1**, **2** corresponds to each of the first and second pumps. A flow rate of the first pump is larger than a flow rate of the second pump in the same manner as that of the first example.

[0090] Each of the first and second plunger pump devices **1**, **2** has the first and second pressurizing chambers **102**, **202** and these pressurizing chambers are liquid-tightly sealed with seals **124**, **224**. Each of the first and second plungers **101**, **201** is arranged at each of the first and second pressurizing chambers **102**, **202**. The first and second plungers **101**, **201** are slidably held by the bearings **123**, **223**.

[0091] A suction passage **103** and a discharging passage **104** are connected to the first pressurizing chamber **102**. The suction passage **103** is connected to the storing tank **51-1** through the suction pipe **16-1** and the deaeration device **14-1**. The suction passage **103** is provided with the suction check valve **105**. The discharging passage **104** is connected to the discharging pipe **19**. The discharging passage **104** is provided with the discharging check valve **106**.

[0092] The suction passage **203** and the discharging passage **204** are connected to the second pressurizing chamber **202**. The suction passage **203** is connected to the storing tank **51-2** through the suction pipe **16-2** and the deaeration device **14-2**. The suction pipe **203** is provided with the suction check valve **205**. The discharging passage **204** is connected to the discharging pipe **19**. The discharging passage **204** is provided with the discharging check valve **206**.

[0093] Next, a pump operation in the liquid feeding system will be described. Under the air bubble discharging and eluate filling mode, the drain valve **9** is "opened", the two plunger devices are operated and air bubbles in each of the pressurizing chamber and the passage are discharged. Under the starting operation, the drain valve **9** is closed and only the first plunger **101** is operated. A flow rate of the first plunger **101** is larger than a flow rate of the second plunger **201**. Accordingly, the pump discharging pressure easily reaches up to the target pressure. When the pump discharging pressure reaches up to the target pressure, the operation is changed from the starting operation to the normal operation. Under the normal operation, the drain valve **9** is closed, the first plunger pump device is stopped and only the second plunger device is operated. The second plunger is pushed into the second pressurizing chamber **202** at a slow speed. With such an operation as above, it is possible to accomplish the predetermined pump flow rate while holding the pump discharging pressure to the target pressure. In addition, although the discharging side of the pump in the preferred embodiment is provided with the discharging check valve, the aforesaid active valve may be applied.

[0094] The two pumps are separately arranged at the liquid feeding system in this example and both of them are connected by the pipe. Accordingly, a disassembling work for the pump becomes easy and maintenance work such a seal replacement work becomes easy. In addition, it can attain advantages that a layout characteristic of equipment is improved.

1. A liquid feeding system having first and second pumps with plungers, a suction port and a discharging port so as to suck liquid through said suction port and to discharge said liquid out of said discharging port under operation of said first and second pumps, wherein under a starting operation mode in which said second pump is stopped and only said first pump is operated, the starting operation mode is changed over to a normal operation mode when a discharging pressure at said discharging port reaches up to a predetermined value, and under the normal operation mode, said first pump is stopped and only said second pump is operated.

2. The liquid feeding system according to claim 1, wherein said predetermined value is equal to a target value of discharging pressure at said discharging port.

3. The liquid feeding system according to claim 1, wherein said predetermined value is lower than a target value of discharging pressure at said discharging port under the normal operation mode.

4. The liquid feeding system according to claim 1, wherein an operation speed of said first pump is reduced when the discharging pressure at said discharging port reaches up to a predetermined value under said starting operation mode.

5. The liquid feeding system according to claim 1, wherein under the air bubble discharging and eluate filling mode before said starting operation mode, said first and second pumps repeat a suction stroke and a discharging stroke in a predetermined period and said second pump repeats the suction stroke and discharging stroke by said first pump with a delay of half-period.

6. The liquid feeding system according to claim 1, wherein under the air bubble discharging and eluate filling mode before said starting operation mode, said second pump is stopped and only said first pump is operated.

7. The liquid feeding system according to claim 1, wherein there is provided a drain valve for releasing a discharging pressure at said discharging port, and under said air bubble discharging and eluate filling mode, said drain valve is released.

8. The liquid feeding system according to claim 1, wherein an operating flow rate of said first pump is higher than an operating flow rate of said second pump.

9. The liquid feeding system according to claim 1, wherein there is provided a map for indicating a relation between a discharging pressure target value at said discharging port and a target flow rate, when said target value is inputted, the target flow rate is calculated in reference to said map, the most-suitable value of a coefficient α of flow rate acting as a ratio between an operating flow rate of said first pump and an operating flow rate of said second pump is calculated in response to said target flow rate.

10. A liquid feeding system having a first pump, a second pump with plungers, a valve device and a discharging port so as to discharge solution from a source of solution out of said discharging port through said first and second pumps, said valve device has two states, i.e. an opened state where said source of solution and said first pump are connected and said first pump and said second pump are shut off and a closed state where said source of solution and said first pump are shut off and said first pump and said second pump are connected, under the starting operation mode, said valve device is set in said opened state, said second pump is stopped, only said first pump is operated, the starting operation mode is changed over to the normal operation mode when the discharging pressure at said discharging port reaches up to a predetermined value, and under the normal operation mode, said valve device is set to said closed state, said first pump is stopped and only said second pump is operated.

11. The liquid feeding system according to claim 10, wherein under the air bubble discharging and eluate filling mode before said starting operation mode, a suction stroke of the first pump is carried out with a delay of ¼ period after said valve device is changed from "opened" state to "closed" state, said valve device is changed from "closed" state to "opened" state with a delay of ¼ upon completion of the suction stroke of the first pump, the suction stroke of the second pump is carried out with a delay of ¼ period after said valve device is changed from "closed" state to "opened" state, a discharging stroke of the first pump is carried out with a delay of ¼ period after said valve device is changed from "opened" state to "closed" state, said valve device is changed from "opened" state to "closed" state with a delay of ¼ upon completion of the discharging stroke of the first pump, and a discharging stroke of the second pump is carried out with a delay of ¼ period after said valve device is changed from "opened" state to "closed" state.

12. The liquid feeding system according to claim 1, wherein a range of liquid feeding flow rate is 0.1 nL/min to 50 μL/min.

13. A gradient operation system having a first liquid feeding device for feeding the first solution, a second liquid feeding device for feeding the second solution, and a mixer for mixing solution fed by said first and second liquid feeding device so as to perform a gradient operation for feeding liquid while a mixing ratio between said first solution and said second solution is being changed in a stepwise manner as time passes by, a feed-back gain proportionate to a ratio between the two liquid feeding flow rates is given to a signal for controlling liquid feeding flow rates of said first and second liquid feeding devices.

14. A gradient operation system having a first liquid feeding device for feeding the first solution, a second liquid feeding device for feeding the second solution, and a mixer for mixing solution fed by said first and second liquid feeding device so as to perform a gradient operation for feeding liquid while a mixing ratio between said first solution and said second solution is being changed in a stepwise manner as time passes by, a feed-back gain proportionate to a ratio between the two liquid feeding flow rates is given to a signal for controlling liquid feeding flow rates of said first and second liquid feeding devices, wherein said first and second liquid feeding devices include the liquid feeding system according to any one of claims 1 to 11.

15. A gradient operation system having a first liquid feeding device for feeding the first solution, a second liquid feeding device for feeding the second solution, and a mixer for mixing solution fed by said first and second liquid feeding device so as to perform a gradient operation for feeding liquid while a mixing ratio between said first solution and said second solution is being changed in a stepwise manner as time passes by, a feed-back gain proportionate to a ratio between the two liquid feeding flow rates is given to a signal for controlling liquid feeding flow rates of said first and second liquid feeding devices, wherein said first and second liquid feeding devices include the liquid feeding system according to claim 12.

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